

IN THE UNITED STATES PATENT
AND TRADEMARK OFFICE

Applicant(s): NISHINO, Shigeyoshi, et al.
Serial No. : 10/583,562
Filed : December 17, 2004
For : PROCESS FOR PREPARING TETRAHYDROPYRAN-4-ONE
AND PYRAN-4-ONE
Art Unit : 1625
Examiner : Bernard Dentz

Hon. Commissioner of Patents
and Trademarks
Alexandria, Virginia 22313-1450

DECLARATION UNDER 37 CFR 1.132

S I R :

I. I, Hidetaka SHIMA, a citizen of Japan, who declares
and says that:

I am an inventor of the present U.S. Patent Applica-
tion as identified above and understand the English
language. I studied the Official Action dated September
11, 2009 received in said application, and in order to show
the utility of the process claimed in the present applica-
tion, the following experiments were carried out under my
supervision.

II. Experiments

Example 5 (Synthesis of tetrahydropyran-4-one)

In a flask made of glass having an inner volume of 20
ml and equipped with a stirring device, a thermometer, a
reflux condenser and a balloon filled with hydrogen were
charged 577 mg (6.0 mol) of pyran-4-one, 120 mg (50% wet
product; containing 0.03 mmol as a palladium atom) of 5% by
weight palladium/carbon, 5 ml of toluene and 1 ml of
ethanol, and the mixture was reacted under hydrogen

atmosphere at room temperature for 3 hours with stirring. After completion of the reaction, the reaction solution was analyzed by gas chromatography (Internal standard method), 513 mg (Reaction yield: 85.4%) of tetrahydropyran-4-one was found to be formed.

Comparative example 1 (Cornubert et al.)

According to Cornubert et al., the experiment was carried out as follows.

That is, 10 g of pyran-4-one and a catalytic amount of Raney nickel were added to 100 cm³ of alcohol (ethanol) and hydrogenation was carried out at the normal pressure and cooling by passing 7250 cm³ of hydrogen for 3 hours.

After completion of the reaction, the reaction mixture was analyzed and found that 6 g of tetrahydropyran-4-one (yield: 68%) and 3.5 g of tetrahydropyranol were formed.

Comparative example 2 (Cornubert et al. in combination with Mazzieri et al.)

In the same manner as in Comparative example 1 except for changing the size of the experiment and the solvent, the experiment was carried out.

That is, 1 g (purity: 98%) of pyran-4-one and a catalytic amount (1 g in aqueous slurry) of Raney nickel were added to 10 ml of a mixed solvent (benzene: methanol=10:1 in volume ratio) and hydrogenation was carried out in a hydrogen normal pressure balloon at room temperature for 3 hours while stirring the mixture with a magnetic stirrer.

After completion of the reaction, the reaction mixture was analyzed by gas chromatography (Internal standard method), and 0.556 g of tetrahydropyran-4-one (yield: 55%) was found to be formed.

Comparative example 3 (Fosker et al.)

According to Fosker et al., the experiment was

carried out as follows.

That is, 19.5 g of pyran-4-one was hydrogenated in 200 ml of methanol at atmospheric pressure for one hour using 5% palladium/calcium carbonate (9.0 g) as catalyst. After removal of the catalyst and the solvent, the concentrate was distilled to yield 14.0 g of tetrahydropyran-4-one (yield: 69%).

Comparative example 4 (Fosker et al. in combination with Mazzieri et al.)

In the same manner as in Comparative example 3 except for changing the size of the experiment and the solvent, the experiment was carried out.

That is, 1 g (purity: 98%) of pyran-4-one and 0.46 g of 5% palladium/calcium carbonate were added to 10 ml of a mixed solvent (benzene:methanol=10:1 in volume ratio) and hydrogenation was carried out in a hydrogen normal pressure balloon at room temperature for one hour while stirring the mixture with a magnetic stirrer.

After completion of the reaction, the reaction mixture was analyzed by gas chromatography (Internal standard method), and no tetrahydropyran-4-one (yield: 0%) was found to be formed.

3. Conclusion

From the results of Example 5 and Comparative examples 1 to 4 mentioned above, it would be clear that hydrogenation of the pyran-4-one of the present invention gives good yield as compared with the processes mentioned in the cited references or the combined processes of the cited references.

Thus, even when a mixed solvent is used as disclosed in Mazzieri et al. in combination with the process disclosed in Cornubert et al. or with that of Fosker et al., no good result can be obtained.

Thus, I believe that the process of the present

invention can give the objective compound with good yield and such an excellent effect of the present invention can never be easily expected by those skilled in the art even when the descriptions of the prior art references are combined with each other as pointed out by the Examiner.

IV. I further declare that all statements made herein of my own knowledge are true and that all statements made in information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001, of Title 18 of the United States Code and that such willful false statements may jeopardize the validity of the application or any patent issued thereon.

Dated: Nov. 19, 2009

Hidetaka Shima
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